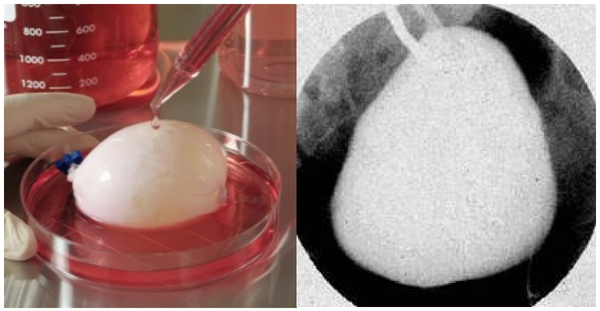
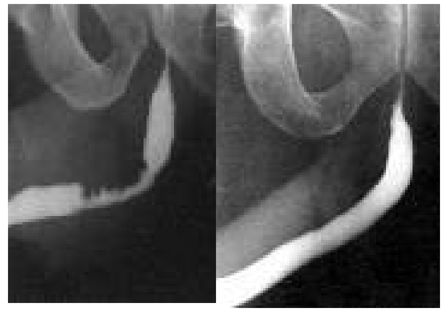
Laboratory-Grown Tissues and Organs

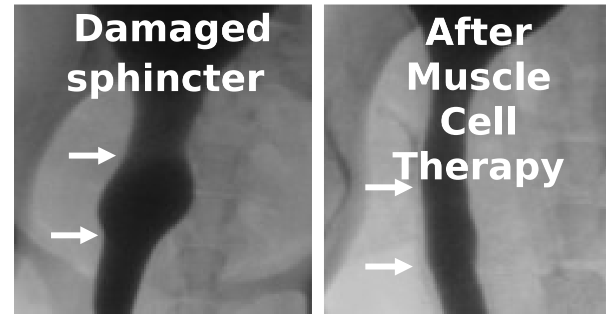
Bladder



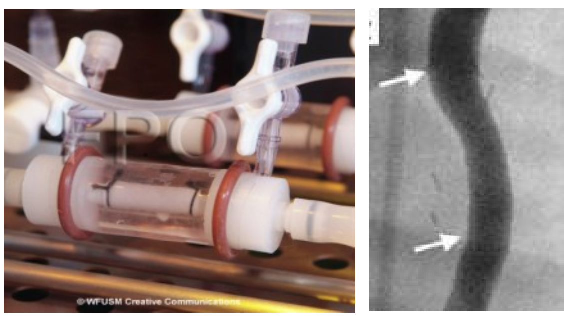
Urethra



Sphincter



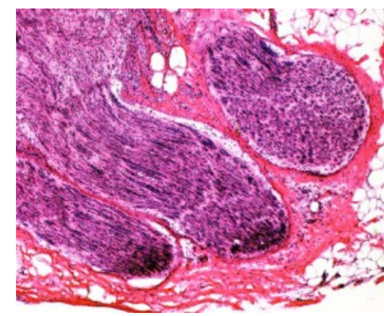
Blood Vessel



Kidney

Heart Valve

Muscle



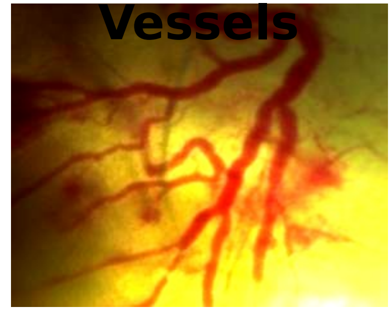
The field of tissue engineering and regenerative medicine is rapidly expanding. Today, we are learning to "build" organs in the laboratory to implant into the human body. For example, patients have already received laboratory-created bladders and urethras as well as injectable cartilage and skin substitutes. Using novel techniques, our team strives to develop methods to engineer other organs, so that those damaged by disease or injury can be replaced. (From the Wake Forest Institute for Regenerative Medicine)

Inkjet Printing Technology and Regenerative Med

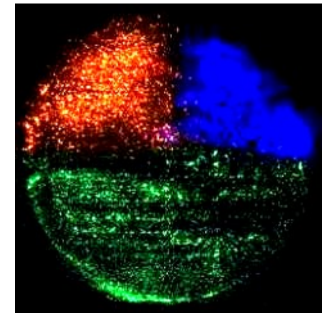
Heart

Bone

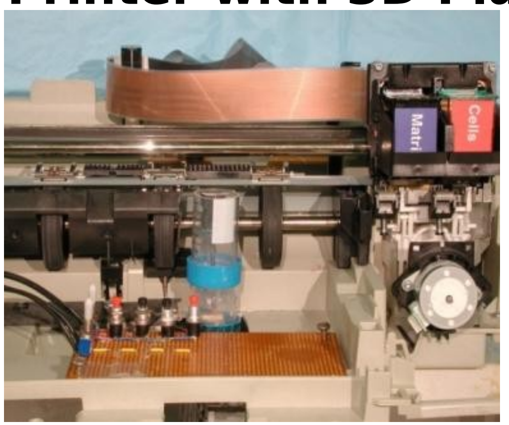
Blood Vessels



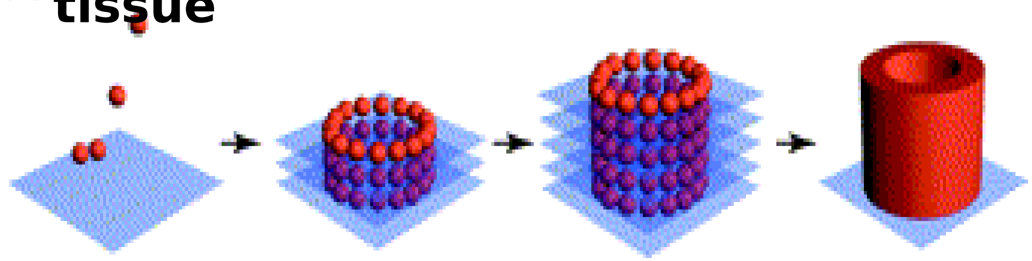
Combined Tissue



Printer with 3D Platform



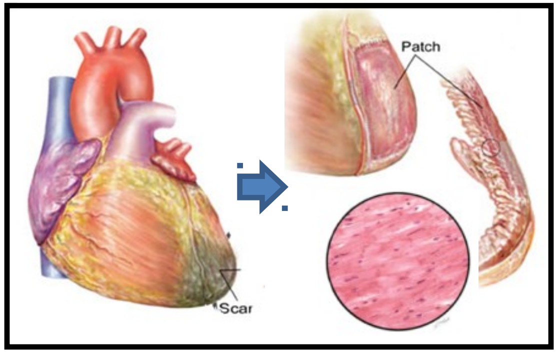
Layer-by-layer assembly of 3-D tissue



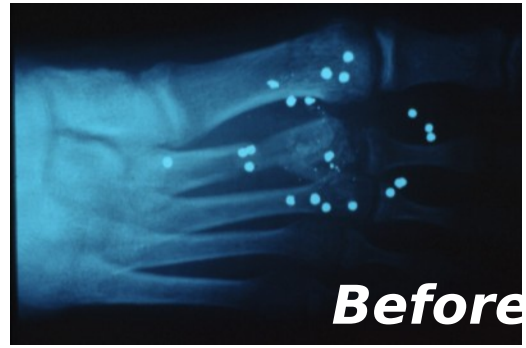
Inkjet printing technology can also be used to engineer organs other than skin. Because the inkjet printer can deliver multiple cell types at a time, and put them in very precise positions, we will be able to build organs that are composed of many different cells and tissues in a completely novel way. We have utilized inkjet printing technology to build heart, bone, and blood vessel tissues. (From the Wake Forest Institute for Regenerative Medicine)

Laboratory-Grown Tissues

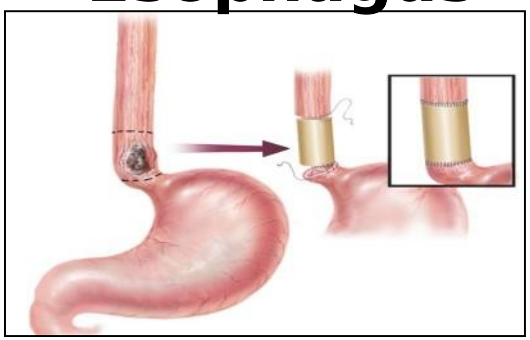
Heart Patch



Shotgun Injury



Esophagus



Shoulder

Some biomaterials obtained from donor tissues contain factors that promote the regenerative process. For example, biomaterials derived from the urinary bladder and intestine of pigs can be used for regeneration of tissues in the body. These materials can attract cells at the injured site, helping with wound healing.

(From the McGowan Institute for Regenerative Medicine)

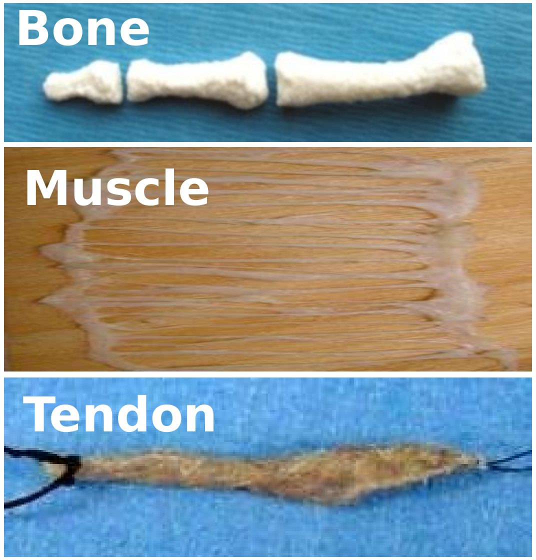
Limb and Digit Restoration

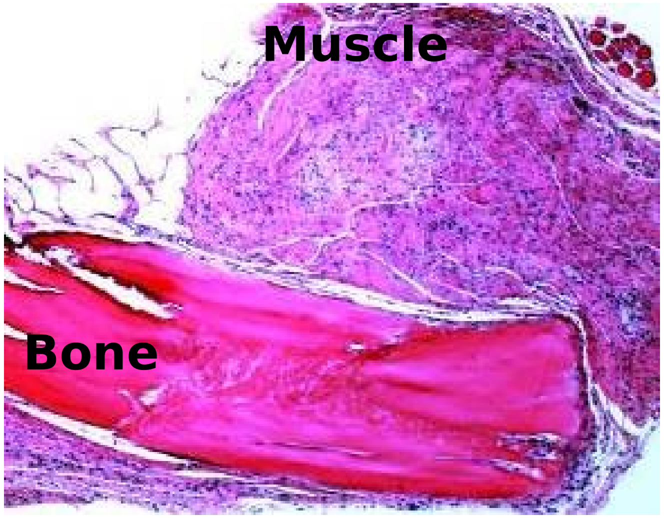
Salamanders are able to regrow limbs – our team is working to harness similar healing powers within the human body. We have developed a powder made from the urinary bladder of pigs, and this material can attract and hold cells at an amputation site, allowing the regenerative process to begin. When this material was used to treat the amputated fingertip of two men (ages 63 and 67), both experienced a rapid restoration of the distal fingertip. The photographs above illustrate the process. We are working to develop this system further, and to understand how it works at a genetic level so that it can be translated to battlefield injuries.
(From the McGowan Institute for Regenerative Medicine)

Laboratory-Engineered Fingers

Components of Digit



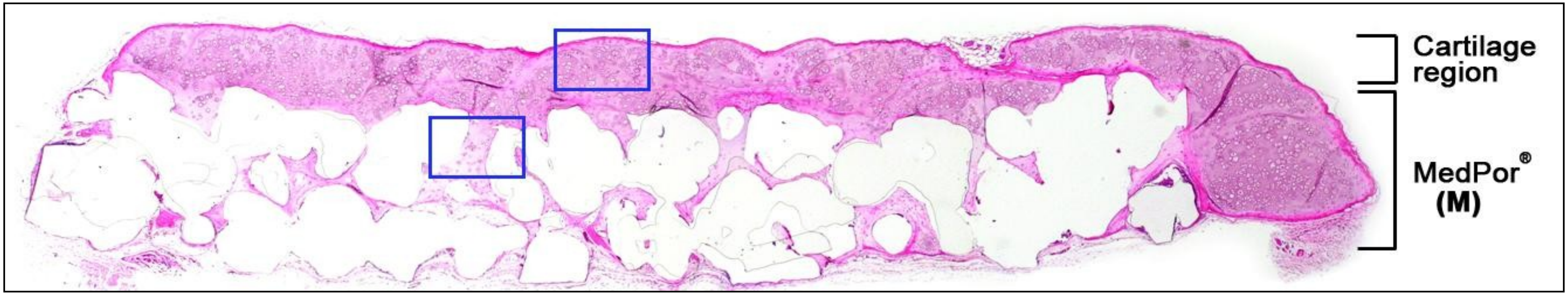
Engineered Tissue



Reconstruction of fingers injured by war trauma is a challenging process. Our goal is to engineer a digit in the laboratory. The finger consists of many different tissue types, including bone, muscle, tendon, cartilage, blood vessels, nerves, connective tissue and skin. Engineering such a complex system is challenging. However, we have demonstrated the feasibility of engineering a digit system that contains bone, muscle and tendon. These different tissue types retained their respective appearance and function. Our next step is to engineer the additional tissues needed for a functional finger.

(From the Wake Forest Institute for Regenerative Medicine)

Ear Reconstruction

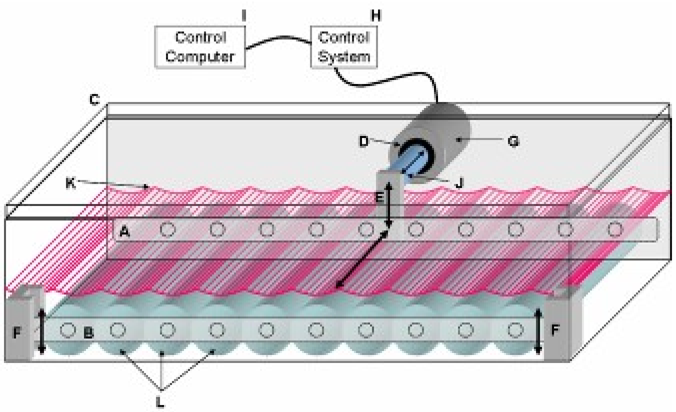


Ear cartilage tissues are frequently injured on the battlefield. Our team has developed a way to grow living cartilage tissue on a synthetic ear-shaped implant in the laboratory. The tissue completely covers the implant and makes it easier to tolerate. The cartilage tissue also helps to maintain the appropriate “ear” shape and the strength of the implant. Thus, the implant may look better and last longer.

A photograph of the synthetic ear-shaped implant is shown above. The microscopic view shows the interface between the implant (white) and the cartilage tissue (pink) illustrating that the cartilage grows smoothly on the surface of the implant and even enters it in places.

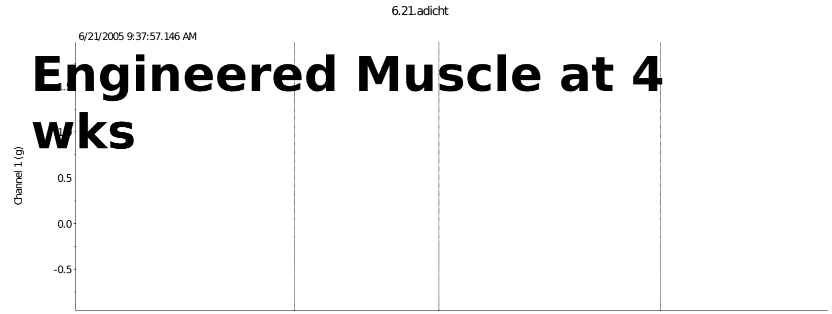
(From the Wake Forest Institute for Regenerative Medicine)

Creating Muscle Tissue in the Lab

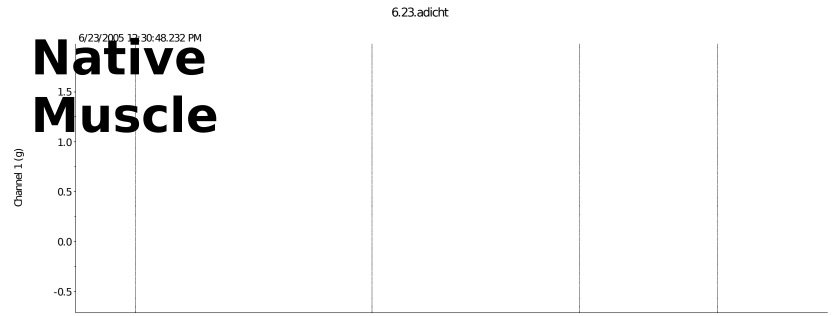


Computer Controlled Bioreactor

Contractility



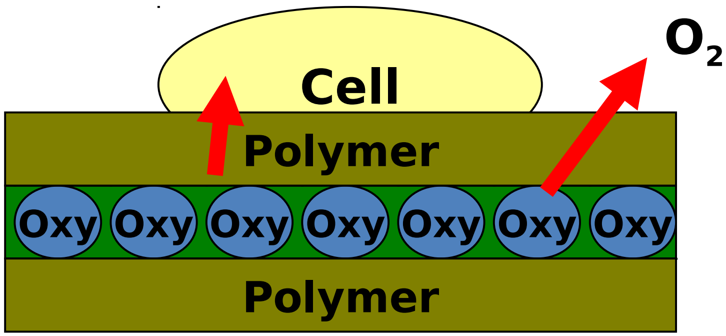
Engineered Muscle at 4 wks



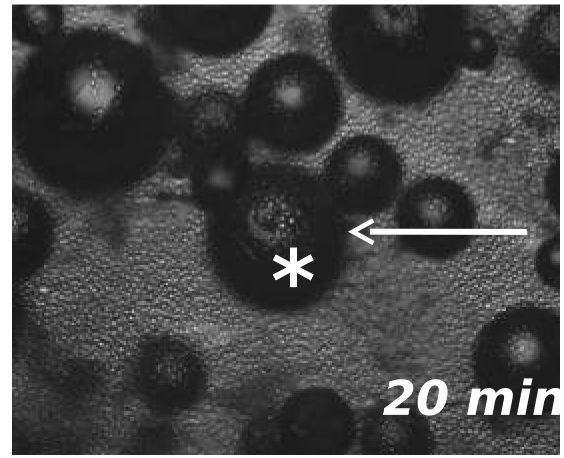
Native Muscle

The inability to build functional muscle tissue remains a major hurdle to reconstructing soft tissue in wounded soldiers. We have developed a computer controlled system to build properly organized muscle tissue in the lab. To do this, human muscle cells are attached to strands of collagen, or connective tissue. They are then subjected to cyclic stretching (“exercise”), in a bioreactor, which is a system designed to simulate the conditions of the human body. Muscle tissues grown this way contracted normally when stimulated with electric current. (From the Wake Forest Institute for Regenerative Medicine)

Oxygen Generating Materials for Building Organs



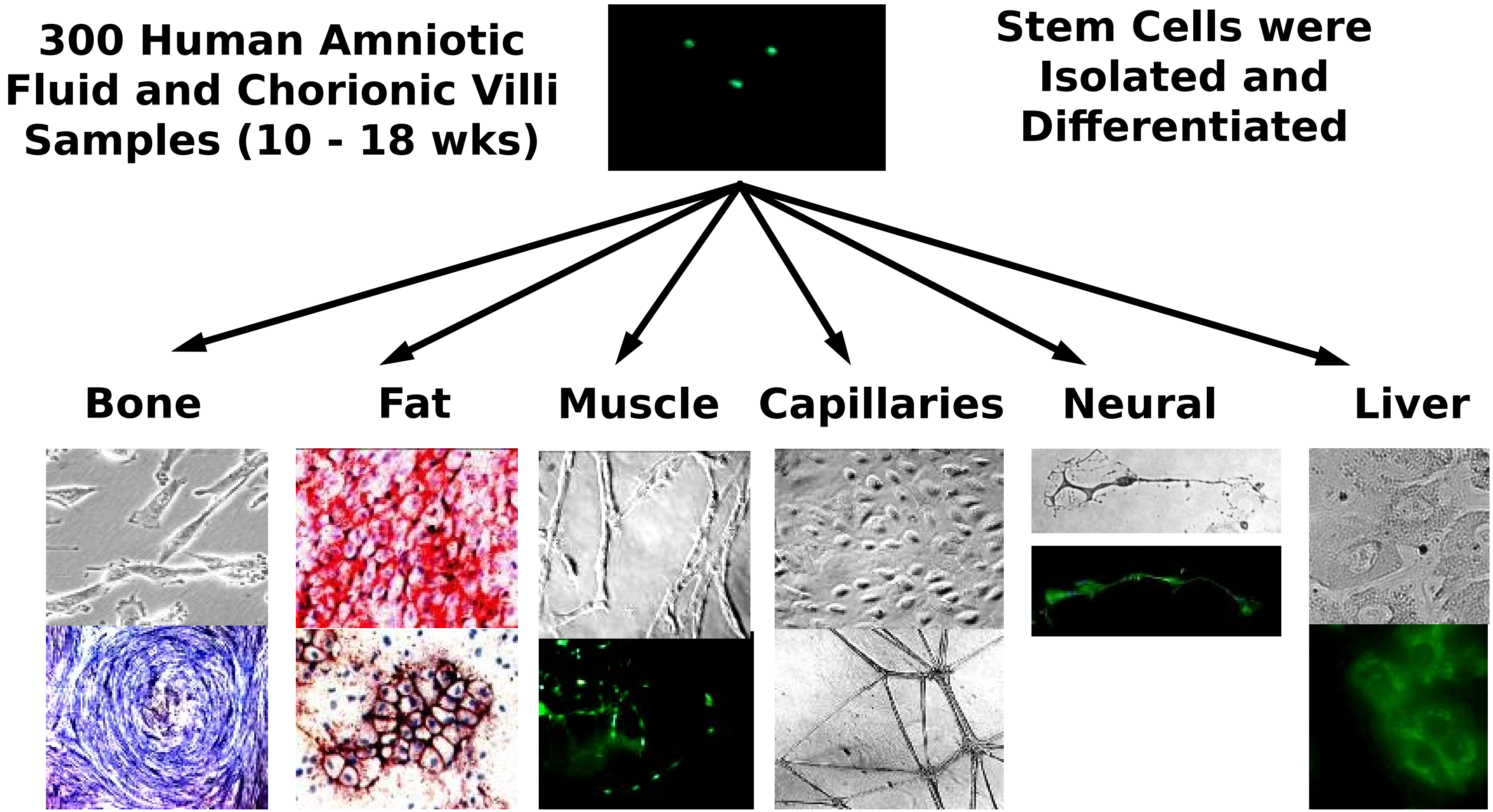
Incorporation of **O_2** generator



To be able to successfully regenerate an organ, enough oxygen must reach the cells and tissues after implantation in the body. This is a significant challenge in the field of tissue engineering. To solve this, we have developed oxygen-generating materials that can be incorporated into the scaffolds used to build an organ. These materials can provide a sustained release of oxygen to cells and tissues to increase their survival time in the body, so that the engineering organ may integrate with the body. This novel system may help speed up clinical applications of tissue engineering.

(From the Wake Forest Institute for Regenerative Medicine)

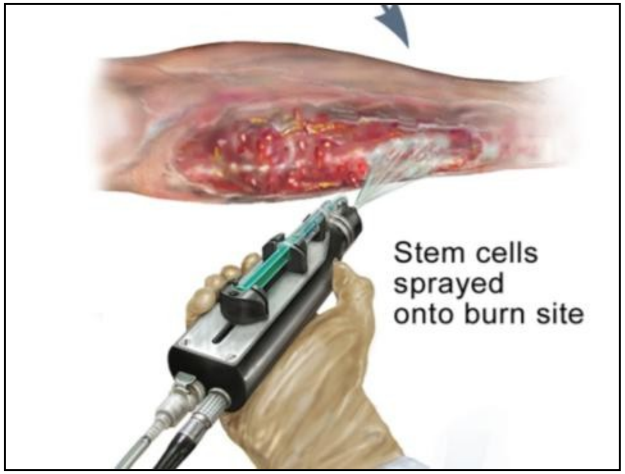
Amniotic Fluid Stem Cells for Tissue Regeneration



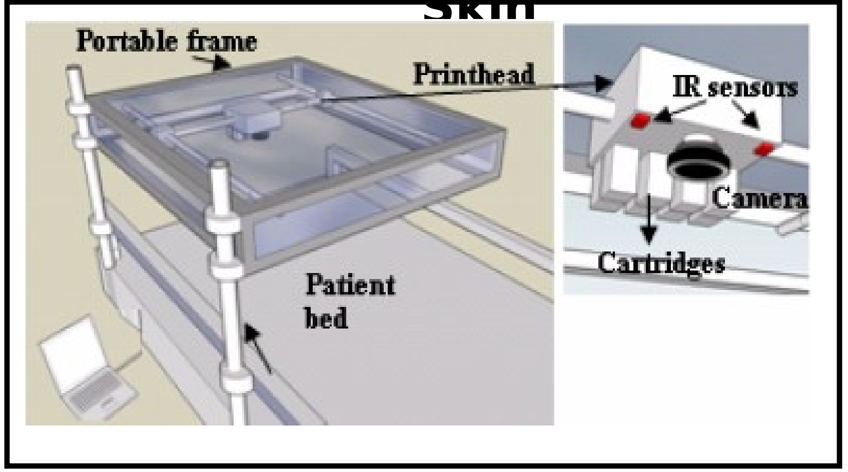
Stem cells are a useful source of cells in instances where a patient's own cells cannot be obtained for regenerative procedures. We have developed a reliable and reproducible source of stem cells from amniotic fluid and placenta. These cells are capable of forming many types of cells, as illustrated above. Because chorionic villi sampling and amniocentesis are routine prenatal testing procedures and do not harm a growing fetus, they could furnish a potentially limitless source of stem cell lines for reconstructive procedures. (From the Wake Forest Institute for Regenerative Medicine)

New Methods for Burn Treatment

Skin Cell Spray Gun



Portable Printer for Skin

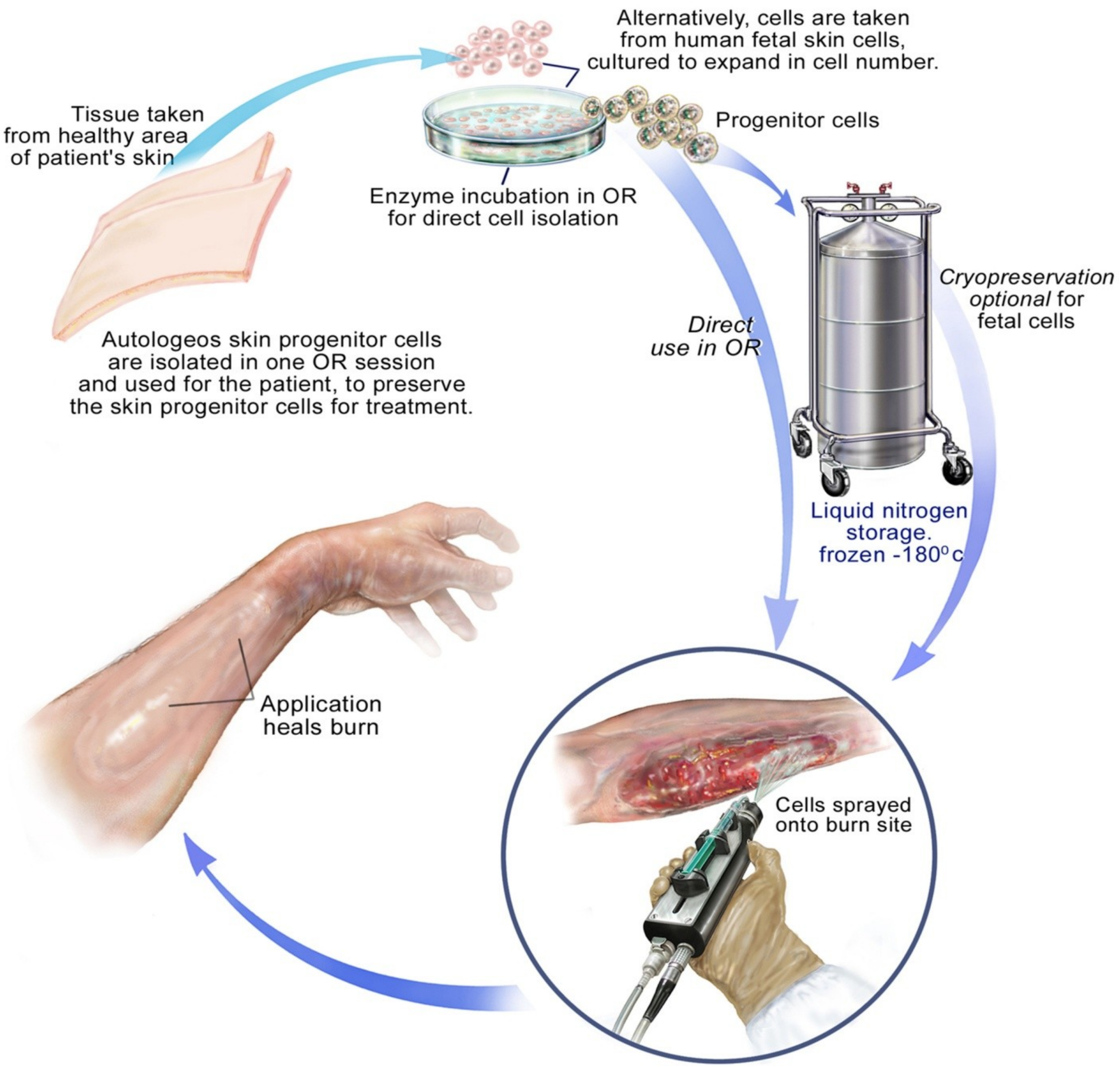


Some soldiers' burns are so extensive, there is not enough undamaged skin to use for grafts. We are taking multiple approaches to solve this problem and have developed the following technologies:

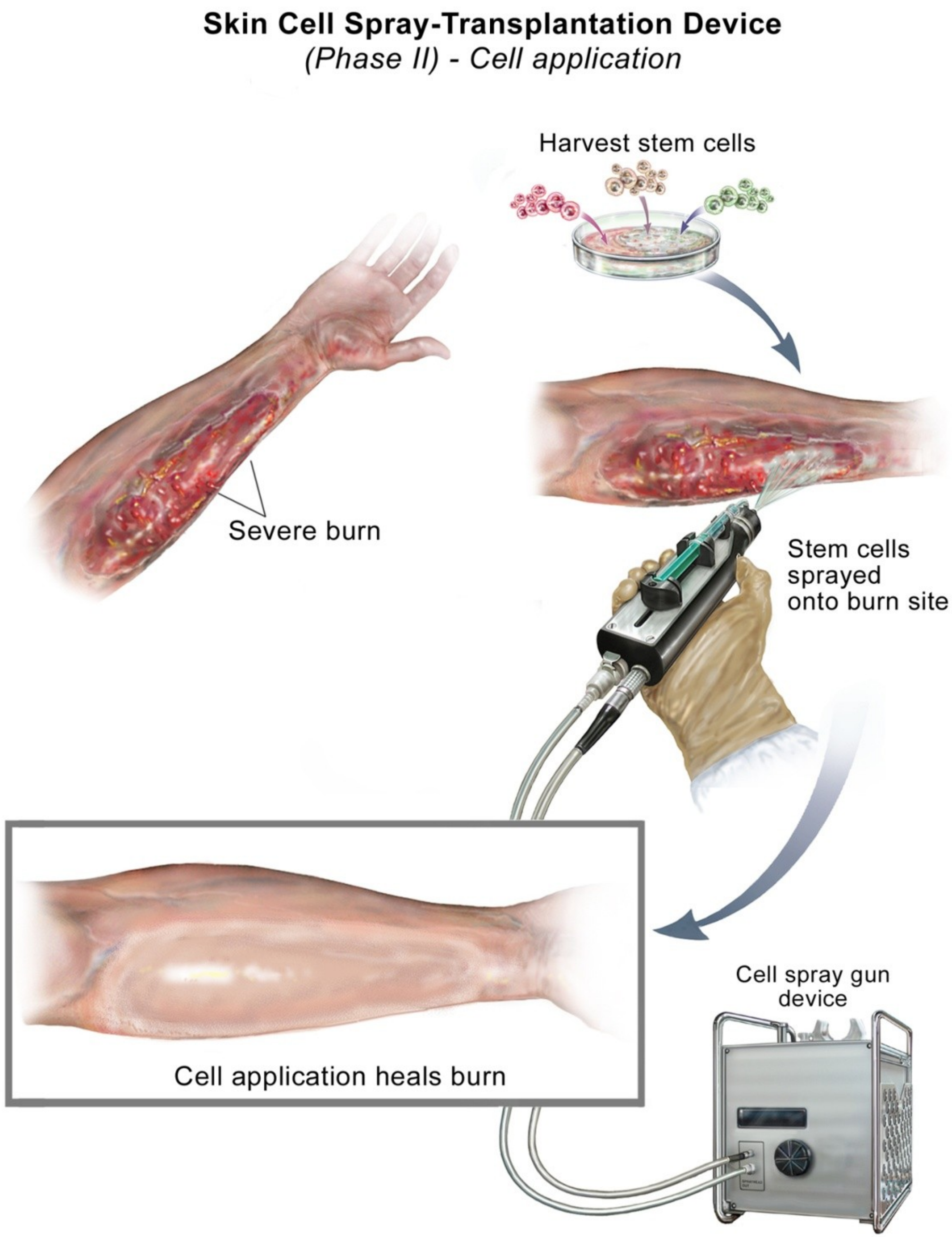
- A spray gun system to evenly deliver keratinocytes, which are the building blocks of skin, to the burned area. These cells, which are found in the outer layer of skin, promote healing. In a clinical study involving 16 patients, keratinocytes were taken from patients, grown in large numbers in the laboratory, and then sprayed onto burns. The patients all showed excellent healing after 5 to 9 days.
- An adapted ink-jet printer to provide on-site "printing" of skin for soldiers with life-threatening burns. Skin cells are placed in the sterilized ink cartridge, along with a material to support them, and are printed directly on the wound.

(From the Wake Forest and McGowan Institutes for Regenerative Medicine)

Cell Biology Approach
(Phase I) - Cell harvest



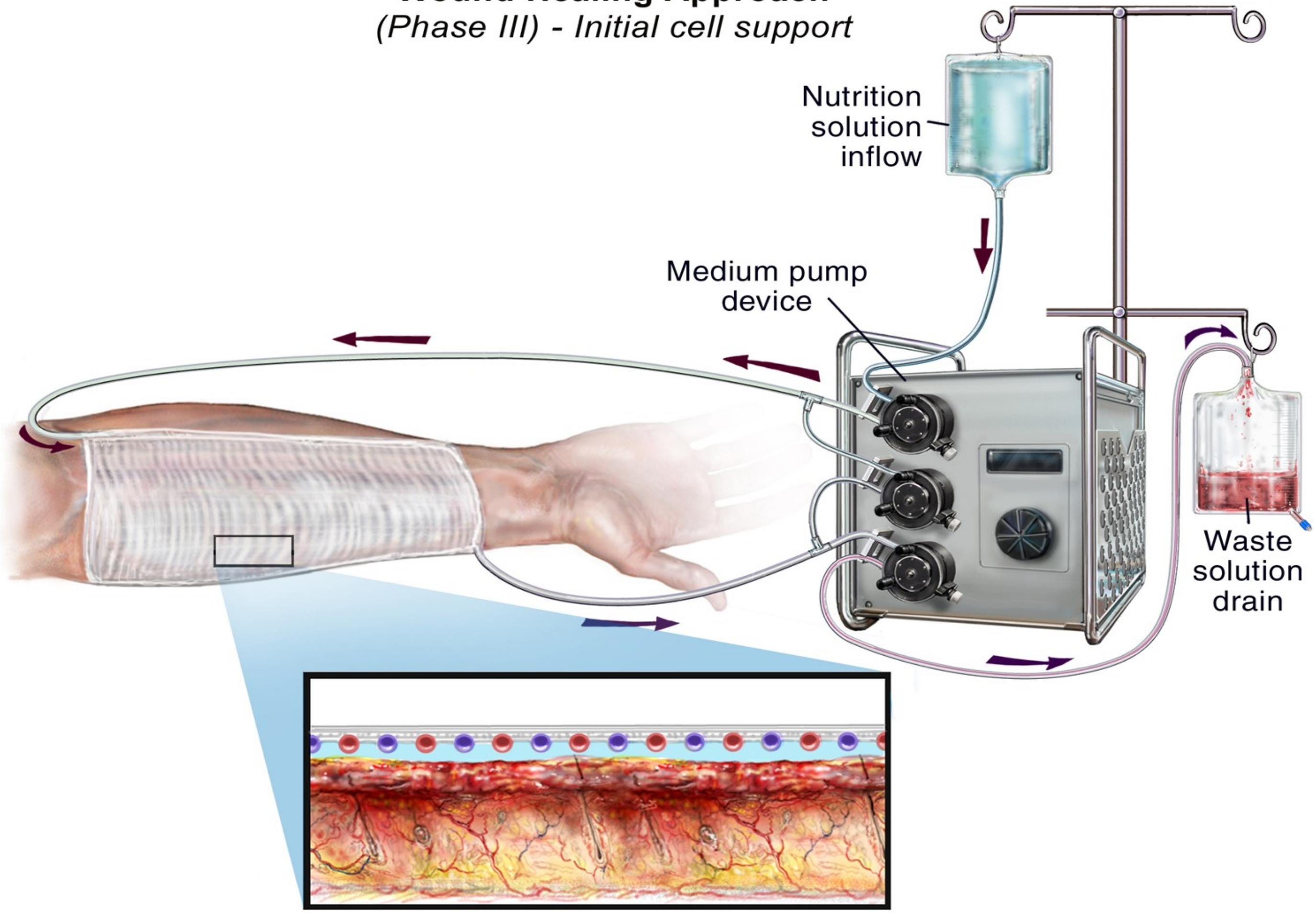
(From the McGowan Institute for Regenerative Med



(From the McGowan Institute for Regenerative Med

Wound Healing Approach

(Phase III) - Initial cell support

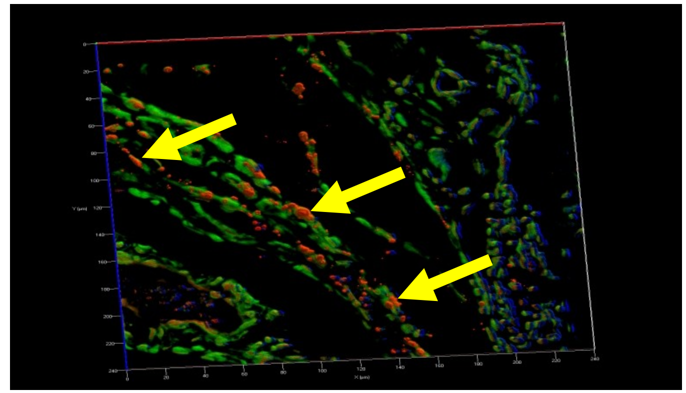


Cross-section view of severe burn.
Artificial capillaries on wound surface, covered with a sealing wound dressing to provide active wound support (arterio-venous hollow fiber membrane system).

(From the McGowan Institute for Regenerative Med

Battlefield Relevant Compartment Syndrome Treatment

Automated muscle and bone marrow stem cell Separation

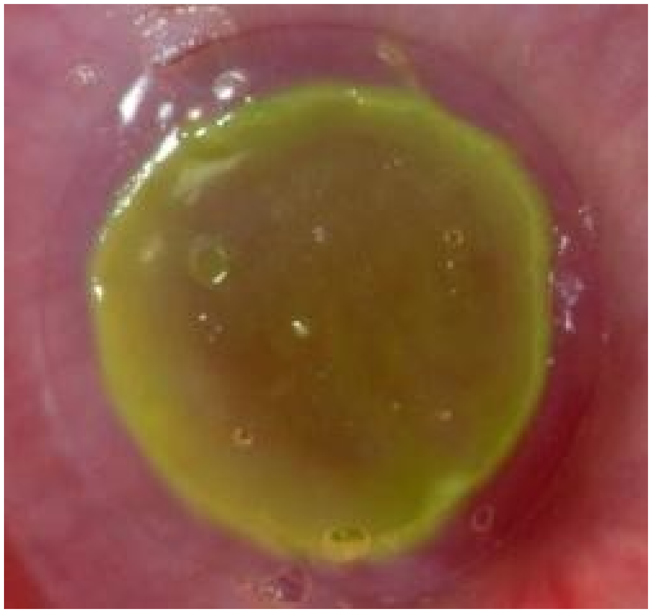


Q-Dot Labeled Cell Engraftment

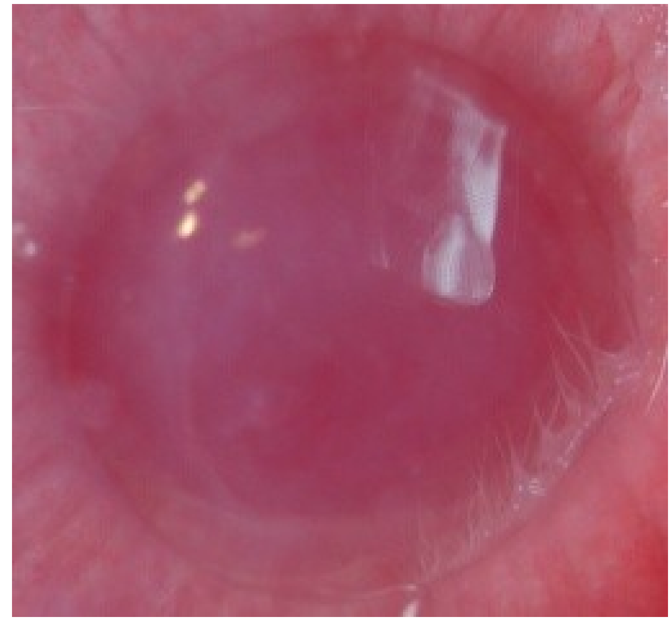
Compartment syndrome occurs when there is sufficient swelling to compromise tissue vascularity and viability. It can lead to major tissue loss and subsequent functional deficiency. Work being done through AFIRM will use regenerative medicine techniques with different cell populations to maximize tissue survival and function. (From the Oregon Biomaterial Engineering Institute, and the Wake Forest and McGowan's Institutes for

Tissue Building Substrates (Lens)

Post-Op Day 0

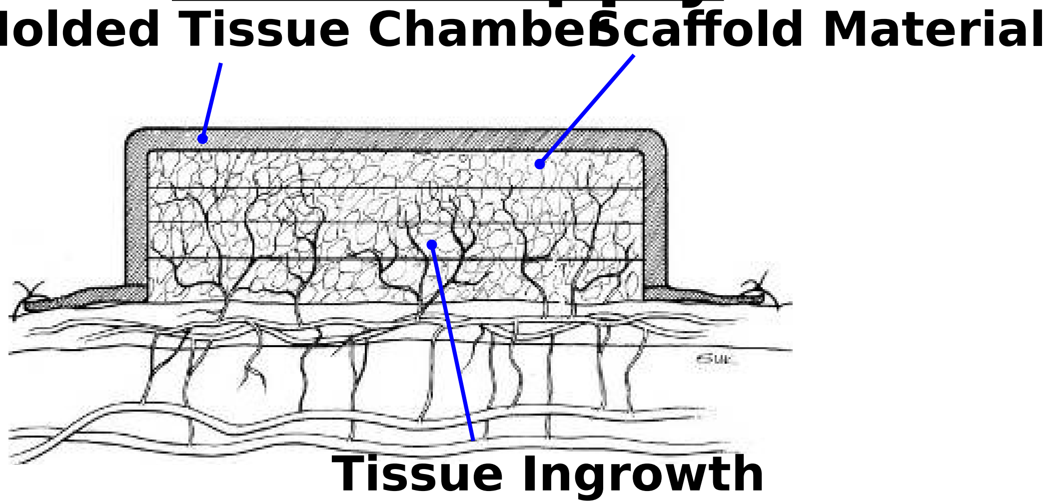


Post-Op Day 7



Tissue building substrates or extracellular matrix (ECM) is an important component of human tissue. It has many functions, ranging from structural support to the guidance of cell growth. We have developed various substrate systems that improve tissue formation in the laboratory. In this particular study, we used an artificial substrate to repair the lens of the eye. We show that these artificial ECM proteins are strong enough for implantation in animals and that they support repair within 7 days after implantation in the cornea. Artificial ECM proteins are designed by combining elements found in natural ECM, such as fibronectin, collagen, laminin and elastin. These ECM proteins can be used in many AFIRM applications. These photographs show artificial ECM lenses in the rabbit eye. The green color on the left comes from a solution of fluorescein dye, which is dropped on the eye to facilitate identification of the edge of the epithelium and determine wound size. At seven days, the wound is closed (right). (From the

Growing Bone Tissue with Its Own Blood Supply



Current techniques for bone reconstruction rely on harvesting bone tissue from elsewhere in the body, a procedure that creates a second bone injury. To avoid this, scientists have attempted to use synthetic materials and cadaver bones as implants, but the results have been disappointing. Problems include the materials being rejected by the body or the implant failing to develop a blood supply and failing. We have developed an alternative approach, in which “donor” bone for reconstruction purposes was generated from the rib cage. Two chambers made of a special material were filled with particles of bone. After being implanted in an animal model, the chambers produced molded blocks of bone tissue that had their own blood supply, just as normal bone does. This discovery suggests the possibility of making customized replacement bone for battlefield injuries as well as treating other types of skeletal injuries or defects that cannot be repaired today. (From Rice University and the University of Texas-Houston)

Hand Transplantation

Hand transplantation is now a reality and 37 of these operations have been performed over the past 8 years. Despite remarkable results, the surgery is not widely used because of side effects from the powerful drugs that must be taken to prevent the body from rejecting the new hand. Our team is developing a way to suppress the immune system with fewer drugs, which will allow transplants of many organs, not just the hand, without rejection.

(From the McGowan Institute for Regenerative Medicine)